REMARKS

In the Final Action dated January 24, 2005, claims 1, 3-7, 11 and 34 are pending and under examination. Claims 1, 3-7, 11 and 34 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1, 3-7 and 11 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent 6,329,145 to Janjic et al. ("Janjic"). Further, claim 34 is rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Janjic in view of U.S. Patent 5,863,753 to Haugland et al. ("Haugland").

This Response addresses each of the Examiner's rejections and objections. Applicants respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 1, 3-7, 11 and 34 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

In response, Applicants have amended independent claim 1 to correct a typographical error. It is respectfully submitted that the claims, as presently recited, are not indefinite. Withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is therefore respectfully requested.

Claims 1, 3-7 and 11 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent 6,329,145 to Janjic et al. ("Janjic").

According to the Examiner, Janjic teaches a competitive binding assay for identifying a compound based on its ability to compete with a nucleic acid ligand. The Examiner also contends that Janjic teaches immobilizing molecules on a solid support and contacting samples containing a non-nucleic acid molecule (see Abstract; Col. 6, line 33-46; and Figures 1-3). Further, the Examiner alleges that Janjic teaches measuring the competition of the candidate

compound to displace the binding partner of the immobilized nucleic acid complex, wherein the change or alteration of the binding, e.g., inhibition or dissociation of the binding partner to the immobilized nucleic acid, is an indication of the presence of the compound.

Applicants respectfully submit that the Examiner's characterization of Janjic's disclosure is inaccurate, and that Janjic's disclosure is directed to an entirely different methodology.

Applicants respectfully submit that Janjic relates to a new application of the SELEX technology. Applicants respectfully direct the Examiner's attention to attached **Exhibit 1**, which graphically depicts the general steps of the SELEX methodology, consistent with the description in the Background section of Janjic. In essence, the SELEX methodology provides a library of synthetic nucleic acid molecules (i.e. aptamers), which library is enriched for those nucleic acid molecules having an ability to bind to a particular non-nucleic acid target molecule.

Janjic relates to a new application of a nucleic acid library enriched for the ability to bind a particular target. On column 3, "Summary of the Invention", Janjic states that the invention is directed to the use of aptamers (i.e. the *enriched* nucleic acid library for a particular target) to identify compounds that displace the aptamers from their targets. Further, claim 1 of Janjic delineates the method as screening for a compound from a library of compounds for the ability of the compound to displace, through competition, a labeled nucleic acid from a complex formed between the nucleic acid and the target. Therefore, the objective of the method disclosed and claimed by Janjic is to find compounds that compete with a nucleic acid in binding to a target.

Throughout the disclosure of Janjic, there is no specific teaching or exemplification of target compounds that are nucleic acid molecules. At col. 4, lines 38-42, Janjic provides a

laundry list of target compounds, none of which is a nucleic acid. Two specific examples of target compounds are given in column 4, lines 5 to 10 of Janjic, i.e., platelet-derived growth factor (PDGF) and wheat germ agglutinin (WGA). Aptamers are prepared and enriched for binding to PDGF or WGA. PDGF and WGA form a complex with their respective aptamers, and compounds are screened to identify those that can displace the aptamers and bind to PDGF and WGA, respectively.

Notably, in Janjic's method, the compounds identified by Janjic bind to a non-nucleic acid target molecule (e.g., PDGF and WGA), not to the nucleic acid aptamers. The nucleic acid aptamer is displaced by a candidate compound from a complex formed between the nucleic acid aptamer and the target molecule (such as PDGF and WGA).

Applicants respectfully submit that Janjic's method is fundamentally different from the method of the presently claimed invention, where a toxicant is identified on the basis that it binds to a nucleic acid molecule and inhibits the binding of the nucleic acid molecule to a binding partner, such as a dye. Therefore, it is the binding partner of the nucleic acid molecule (such as a dye), not the nucleic acid molecule, that is being displaced or disassociated from a complex formed between the nucleic acid and the binding partner, as a result of the presence of the toxicant. For example, the specification describes that in one embodiment, a dye forms a complex with a nucleic acid molecule – i.e., the binding partner of the nucleic acid in this instance is the dye. The dye in the complex fluoresces. A toxicant molecule, if present in the sample to be tested, would bind to the nucleic acid molecule and causes structural changes of the nucleic acid molecule, e.g., breaking of the base pairs or causing such a change in conformation, leading to the release of the dye or quenching of the florescent signal. In other words, the subject invention is directed to identification of a toxicant that binds to a nucleic acid, unlike the

identification of a compound which binds to a target molecule such as PDGF by competing with and displacing a nucleic acid molecule (aptamer) in Janjic.

To highlight the distinguishing features of the present invention, Applicants have amended independent claim 1 and added claims 35-37. Support for the amendment to claim 1 is found throughout the specification, e.g., on page 8, lines 24-28, and page 19, Example 9. Support for new claims 35-37 is found in previous claim 1 and in the specification. No new matter is introduced. Specifically, the claims as presently recited define the toxicant to be detected as a molecule "which binds to a nucleic acid molecule" (see independent claims 1, 35 and 36), and the detection of the toxicant is based on dissociation of binding between the nucleic acid molecule and a binding partner of said nucleic acid molecule, or inhibition of binding of a binding partner to the nucleic acid molecule.

In view of the foregoing, Applicants respectfully submit that Janjic does not anticipate the claimed invention. Withdrawal of the rejection under 35 U.S.C. §102(e) based on Janjic is therefore respectfully requested.

Claim 34 is rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Janjic in view of U.S. Patent 5,863,753 to Haugland et al. ("Haugland").

The Examiner concedes that Janjic does not teach using a dye for detection. However, the Examiner contends that Haugland teaches conjugating a chemical cyanine dye on the nucleic acid for enhancement of fluorescence-sensitivity of detection of DNA binding. Therefore, the Examiner concludes that it would have been obvious to one skilled in the art, at the time the invention was made, to employ the chemical dye as taught by Haugland in the detection of DNA binding in an assay disclosed by Janjic, because conjugating with a fluorescent dye is known to increase detection sensitivity.

As submitted above, Janjic fails to teach detection of a toxicant based on its ability to bind to a nucleic acid molecule, which causes the dissociation or inhibition of binding between the nucleic acid molecule and a binding partner of the nucleic acid molecule. In this regard, Applicants respectfully submit that Haugland does not cure the deficiency of Janjic at all. Therefore, Applicants respectfully submit that the combination of Janjic and Haugland does not render the claimed methods obvious. Accordingly, the rejection under 35 U.S.C. §103(a) based on Janjic in view of Haugland is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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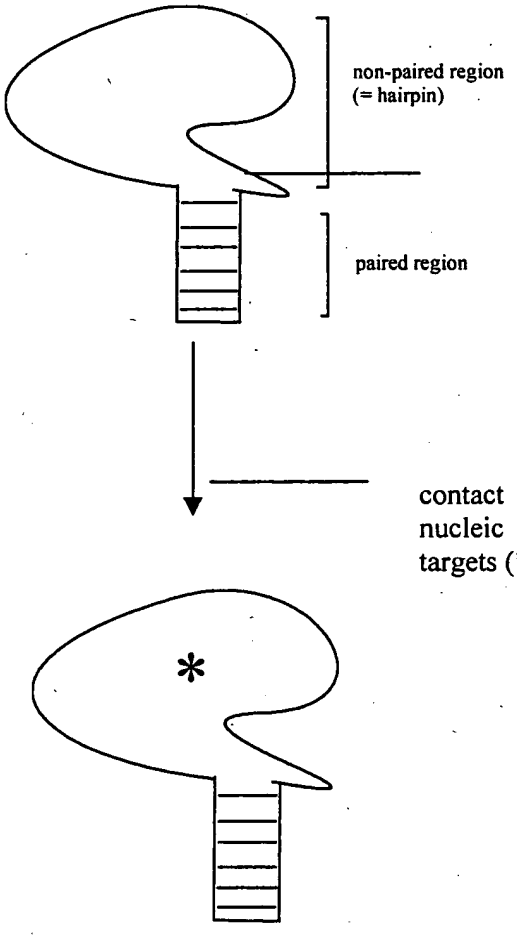
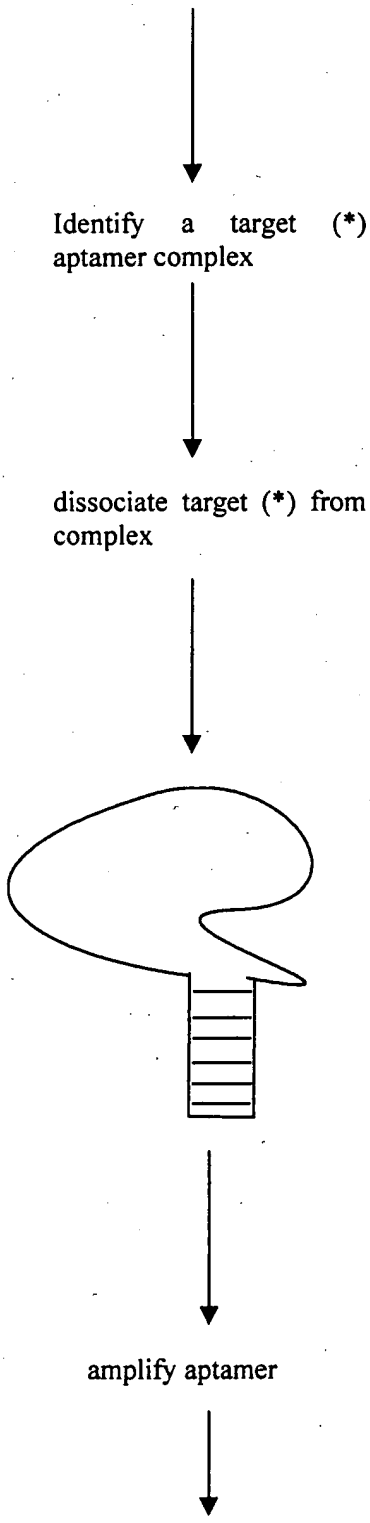
Encl.: Exhibit 1

Generate synthetic library of oligonucleotides which generate a hairpin of variable conformation.

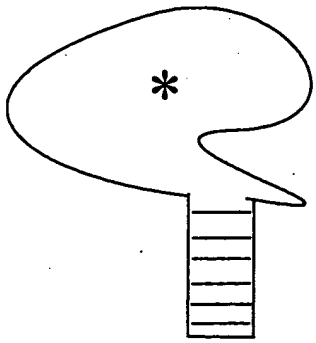


contact library with non-nucleic acid potential targets (*)


Identify a target (*) aptamer complex
dissociate target (*) from complex
amplify aptamer

re-contact library with identified target (*)

re-contact amplified aptamer to and select aptamer-target (*)



repeat process to generate a highly enriched library specific for a particular target